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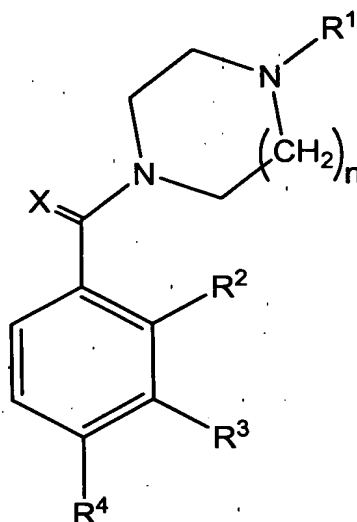
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CLAIMS

What is claimed is:

5

1. A composition comprising a compound of formula (I):



(I)

wherein

10

R¹ is C₁₋₁₀ alkyl, C₃₋₈ alkenyl, C₃₋₈ cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₆ alkyl, (C₃₋₈ cycloalkyl)C₃₋₈ alkenyl, or (C₁₋₈ alkylcarbonyl)C₁₋₈ alkyl;

n is 1 or 2;

X is O or S;

one of R², R³ and R⁴ is G and the other two independently are

15

hydrogen, fluoro, chloro, bromo, nitro, trifluoromethyl, methyl, or C₁₋₃alkoxy;

G is LQ;

L is unbranched -(CH₂)_m- wherein m is an integer from 1 to 7;

Q is NR⁸R⁹ wherein R⁸ is independently selected from hydrogen, C₁₋₆

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alkyl, C₃₋₆ alkenyl, 3-9 membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (6-9-membered heterocyclyl)C₁₋₆ alkylene, and (phenyl)C₁₋₆ alkylene; and R⁹ is independently selected from C₁₋₆ alkyl, C₃₋₆ alkenyl, 6-9 membered carbocyclyl, 3-12

membered heterocyclyl, phenyl, (6-9-membered heterocyclyl) C_{1-6} alkylene, and (phenyl) C_{1-6} alkylene; or

Q is a saturated 3-12 membered N-linked heterocyclyl, wherein, in addition to the N-linking nitrogen, the 3-12 membered

5 heterocyclyl may optionally contain between 1 and 3 additional heteroatoms independently selected from O, S, and NH;

wherein Q is optionally substituted with 1-3 substituents independently

10 selected from the group consisting of hydroxy, halo, carboxamide, C_{1-6} alkyl, 5-9 membered or 6-9 membered heterocyclyl, -N(C_{1-6} alkyl)(5-9 membered or 6-9 membered heterocyclyl), -NH(5-9 membered or 6-9 membered heterocyclyl), -O(5-9 or 6-9 membered heterocyclyl), (5-9 membered or 6-9 membered heterocyclyl) C_{1-3} alkylene, C_{1-6} alkoxy, (C_{3-6} cycloalkyl)-O-, phenyl, (phenyl) C_{1-3} alkylene, and (phenyl) C_{1-3} alkylene-O-, where each of above heterocyclyl, phenyl, and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, methoxy, halo, nitro, cyano, hydroxy, and C_{1-3} alkyl;

provided however that when R^1 is methyl, G is not piperidin-1-ylmethyl;

20 and

wherein each of the above alkyl, alkylene, alkenyl, heterocyclyl, cycloalkyl, carbocyclyl, and aryl groups may each be independently and optionally substituted with between 1 and 3 substituents independently selected from trifluoromethyl, methoxy, halo, amino, nitro, hydroxy, and C_{1-3} alkyl;

25 or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.

2. A compound of claim 1, wherein R^1 is C_{1-10} alkyl.

30

3. A compound of claim 1, wherein R^1 is C_{3-5} alkyl.

4. A compound of claim 1, wherein wherein R^1 is isopropyl.

5. A compound of claim 1 wherein n is 1.
6. A compound of claim 1, wherein wherein X is O.
- 5 7. A compound of claim 1, wherein one of R³ and R⁴ is G.
8. A compound of claim 1, wherein R⁴ is G.
- 10 9. A compound of claim 1, wherein L is unbranched -(CH₂)_m-, wherein m is an integer from 1 to 4.
10. A compound of claim 1, wherein L is -CH₂-.
- 15 11. A compound of claim 1, wherein L is -CH₂CH₂-.
12. A compound of claim 1 wherein Q is a saturated N-linked nitrogen-containing heterocycl.
- 20 13. A compound of claim 1, wherein Q is selected from substituted or unsubstituted piperidinyl, diazepanyl, azepanyl, decahydroisoquinolin-2-yl, piperazinyl, pyrrolinyl, pyrrolidinyl, thiomorpholinyl, or morpholinyl.
- 25 14. A compound of claim 1, wherein Q is unsubstituted piperidinyl, diazepanyl, azepanyl, decahydroisoquinolin-2-yl, piperazinyl, pyrrolinyl, pyrrolidinyl, thiomorpholinyl, or morpholinyl.
15. A compound of claim 14, wherein Q is unsubstituted diazepanyl, azepanyl, morpholinyl, decahydroisoquinolin-2-yl, piperidinyl, or pyrrolidinyl;
- 30

16. A compound of claim 1, wherein substituted Q are selected from N-(C₁₋₆ alkyl)piperazinyl, N-phenyl-piperazinyl, 1,3,8-triaza-spiro{4.5}deacyl, and 1,4-dioxa-8-aza-spiro{4.5}deacyl.
- 5 17 A compound of claim 1, wherein Q is a monovalent radical of an amine selected from aziridine, 1,4,7-trioxa-10-aza-cyclododecane, thiazolidine, 1-phenyl-1,3,8-triaza-spiro{4.5}decan-4-one, piperidine-3-carboxylic acid diethylamide, 1,2,3,4,5,6-hexahydro-{2,3'}bipyridinyl, 4-(3-trifluoromethyl-phenyl)-piperazine, 2-piperazin-1-yl-pyrimidine, 10 piperidine-4-carboxylic acid amide, methyl-(2-pyridin-2-yl-ethyl)-amine, {2-(3,4-dimethoxy-phenyl)-ethyl}-methyl-amine, thiomorpholinyl, allyl-cyclopentyl-amine, {2-(1H-indol-3-yl)-ethyl}-methyl-amine, 1-piperidin-4-yl-1,3-dihydro-benzoimidazol-2-one, 2-(piperidin-4-yloxy)-pyrimidine, piperidin-4-yl-pyridin-2-yl-amine, phenylamine, pyridin-2-ylamine.
- 15 18. A compound of claim 1, wherein Q is selected from diazepanyl, azepanyl, morpholinyl, piperidinyl, and pyrrolidinyl, optionally substituted with between 1 and 3 substituents selected from hydroxy, halo, carboxamide, C₁₋₆ alkyl, 5-9 membered or 6-9 membered heterocyclyl, - 20 N(C₁₋₆ alkyl)(5-9 membered or 6-9 membered heterocyclyl), -NH(5-9 membered or 6-9 membered heterocyclyl), -O(5-9 or 6-9 membered heterocyclyl), (5-9 membered or 6-9 membered heterocyclyl)C₁₋₃ alkylene, C₁₋₆ alkoxy, (C₃₋₆ cycloalkyl)-O-, phenyl, (phenyl)C₁₋₃ alkylene, and (phenyl)C₁₋₃ alkylene-O-, where each of above heterocyclyl, phenyl, 25 and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, methoxy, halo, nitro, cyano, hydroxy, and C₁₋₃ alkyl.
- 30 19. A compound of claim 12, wherein Q is substituted with a substituent comprising a 5-9 membered heterocyclyl group selected from: pyridyl, pyrimidyl, furyl, thiofuryl, imidazolyl, (imidazolyl)C₁₋₆ alkylene, oxazolyl, thiazolyl, 2,3-dihydro-indolyl, benzimidazolyl, 2-oxobenzimidazolyl,

(tetrazolyl)C₁₋₆ alkylene, tetrazolyl, (triazolyl)C₁₋₆ alkylene, triazolyl, (pyrrolyl)C₁₋₆ alkylene, pyrrolidinyl, and pyrrolyl.

- 5
20. A compound of claim 19, wherein Q is piperidinyl.
21. A compound of claim 1, wherein R⁸ is hydrogen.
22. A compound of claim 1, wherein R⁹ is C₁₋₆ alkyl.
- 10 23. A compound of claim 1, wherein R⁹ is unsubstituted or substituted phenyl.
24. A compound of claim 1, wherein R⁸ and R⁹ independently are C₁₋₆ alkyl.
- 15 25. A compound of claim 1, wherein R⁸ and R⁹ are methyl.
26. A compound of claim 1, wherein R⁸ and R⁹ are ethyl.
- 20 27. A compound of claim 21, wherein R⁹ is selected from phenyl or 5-9 membered aromatic heterocyclyl, wherein said phenyl or aromatic heterocyclyl is optionally substituted with 1-3 substituents selected from methoxy, hydroxy, halo, nitro, cyano, trifluoromethyl, and C₁₋₃ alkyl.
- 25 28. A compound of claim 27, wherein R⁹ is selected from substituted or unsubstituted phenyl, pyridyl, pyrimidyl, furyl, thiofuryl, imidazolyl, (imidazolyl)C₁₋₆ alkylene, oxazolyl, thiazolyl, 2,3-dihydro-indolyl, benzimidazolyl, 2-oxobenzimidazolyl, (tetrazolyl)C₁₋₆ alkylene, tetrazolyl, (triazolyl)C₁₋₆ alkylene, triazolyl, (pyrrolyl)C₁₋₆ alkylene, pyrrolidinyl, and pyrrolyl.
- 30 29. A compound of claim 28, wherein R⁹ is phenyl.

30. A compound of claim 28, wherein R⁹ is substituted or unsubstituted pyridyl.
31. A compound of claim 1 wherein
- 5 R¹ is C₁₋₁₀ alkyl;
 X is O;
 R⁴ is G;
 L is -CH₂-; and
 Q is a saturated N-linked nitrogen-containing heterocycl.
- 10
32. A compound of claim 31 wherein R¹ is branched.
33. A compound of claim 31 wherein R¹ is C₃₋₅ alkyl.
- 15 34. A compound of claim 31, wherein wherein R¹ is isopropyl.
35. A compound of claim 31, wherein Q is selected from substituted or unsubstituted piperidinyl, diazepanyl, azepanyl, decahydroisoquinolin-2-yl, piperazinyl, pyrrolinyl, pyrrolidinyl, thiomorpholinyl, or morpholinyl.
- 20
36. A compound of claim 31, wherein Q is unsubstituted azepanyl, diazepanyl, morpholinyl, decahydroisoquinolin-2-yl, piperidinyl, or pyrrolidinyl.
- 25 37. A compound of claim 1 selected from the group consisting of:
 (4-[[Ethyl-(2-methoxy-ethyl)-amino]-methyl]-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone;
 (4-Azepan-1-ylmethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
30 (4-Azepan-1-ylmethyl-phenyl)-(4-sec-butyl-piperazin-1-yl)-methanone;
 (4-Azepan-1-ylmethyl-phenyl)-(4-(1-ethyl-propyl)-piperazin-1-yl)-methanone;
 (4-Butyl-piperazin-1-yl)-(4-dimethylaminomethyl-phenyl)-methanone;

(4-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
(4-Butyl-piperazin-1-yl)-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-
phenyl}-methanone;
(4-Butyl-piperazin-1-yl)-{4-[(4-trifluoromethyl-phenylamino)-methyl]-
phenyl}-methanone;
5 (4-Cyclohexyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
(4-Diethylaminomethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone
dihydrochloride;
(4-Dimethylaminomethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone
10 dihydrochloride;
(4-Dimethylaminomethyl-phenyl)-{4-(1-ethyl-propyl)-piperazin-1-yl}-
methanone dihydrochloride;
(4-Isopropyl-piperazin-1-yl)-(3-morpholin-4-ylmethyl-phenyl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(3-piperidin-1-ylmethyl-phenyl)-methanone;
15 (4-Isopropyl-piperazin-1-yl)-(4-[[2-methoxy-ethyl)-propyl-amino]-methyl]-
phenyl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(4-phenylaminomethyl-phenyl)-methanone
dihydrochloride;
20 (4-Isopropyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone
dihydrochloride;
(4-Isopropyl-piperazin-1-yl)-(4-thiomorpholin-4-ylmethyl-phenyl)-
methanone;
25 (4-Isopropyl-piperazin-1-yl)-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-
phenyl}-methanone dihydrochloride;
(4-Isopropyl-piperazin-1-yl)-{4-(4-isopropyl-piperazin-1-ylmethyl)-
phenyl}-methanone;
(4-Isopropyl-piperazin-1-yl)-{4-[(2-methoxy-ethylamino)-methyl]-phenyl}-
30 methanone;
(4-Isopropyl-piperazin-1-yl)-[4-(pyridin-2-ylaminomethyl)-phenyl]-
methanone;

- (4-Isopropyl-piperazin-1-yl)-{4-[(2-methoxy-1-methyl-ethylamino)-methyl]-phenyl}-methanone;
- (4-Isopropyl-piperazin-1-yl)-{4-[(4-trifluoromethyl-phenylamino)-methyl]-phenyl}-methanone;
- 5 (4-Isopropyl-piperazin-1-yl)-{4-[(4-trifluoromethyl-pyridin-2-ylamino)-methyl]-phenyl}-methanone dihydrochloride;
- (4-Isopropyl-piperazin-1-yl)-{4-[(5-trifluoromethyl-pyridin-2-ylamino)-methyl]-phenyl}-methanone dihydrochloride;
- 10 (4-Isopropyl-piperazin-1-yl)-{4-[(6-trifluoromethyl-pyridin-3-ylamino)-methyl]-phenyl}-methanone dihydrochloride;
- (4-Methyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- (4-Methyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone dihydrochloride;
- 15 (4-sec-Butyl-piperazin-1-yl)-(4-dimethylaminomethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- (4-sec-Butyl-piperazin-1-yl)-(4-phenylaminomethyl-phenyl)-methanone;
- 20 (4-sec-Butyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
- {3-(4-Benzyl-piperidin-1-ylmethyl)-phenyl}-(4-methyl-piperazin-1-yl)-methanone;
- 25 {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-phenylaminomethyl-phenyl)-methanone dihydrochloride;
- 30 {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;

- {4-(1-Ethyl-propyl)-piperazin-1-yl}-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
{4-(1-Ethyl-propyl)-piperazin-1-yl}-{4-(decahydro-isoquinolin-2-ylmethyl)-phenyl}-methanone;
5 {4-(1-Ethyl-propyl)-piperazin-1-yl}-{4-((4-trifluoromethyl-phenylamino)-methyl)-phenyl}-methanone dihydrochloride;
{4-(1-Methyl-heptyl)-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
10 {4-(1-Methyl-heptyl)-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
{4-(Benzylamino-methyl)-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
{4-(Benzylamino-methyl)-phenyl}-{4-(1-ethyl-propyl)-piperazin-1-yl}-methanone; and
15 {4-((5-Chloro-pyridin-2-ylamino)-methyl)-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride.
38. A compound of claim 1 selected from the group consisting of:
20 (4-[[Ethyl-(2-methoxy-ethyl)-amino]-methyl]-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone;
(4-Azepan-1-ylmethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
(4-Azepan-1-ylmethyl-phenyl)-(4-sec-butyl-piperazin-1-yl)-methanone;
(4-Azepan-1-ylmethyl-phenyl)-(4-(1-ethyl-propyl)-piperazin-1-yl)-
25 methanone;
(4-Butyl-piperazin-1-yl)-(4-dimethylaminomethyl-phenyl)-methanone;
(4-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
(4-Butyl-piperazin-1-yl)-(4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl)-methanone;
30 (4-Cyclohexyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
(4-Diethylaminomethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;

- (4-Dimethylaminomethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
- (4-Dimethylaminomethyl-phenyl)-{4-(1-ethyl-propyl)-piperazin-1-yl}-methanone dihydrochloride;
- 5 (4-Isopropyl-piperazin-1-yl)-(3-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-[(2-methoxy-ethyl)-propyl-amino]-methyl)-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-phenylaminomethyl-phenyl)-methanone dihydrochloride;
- 10 (4-Isopropyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone dihydrochloride;
- (4-Isopropyl-piperazin-1-yl)-(4-thiomorpholin-4-ylmethyl-phenyl)-methanone;
- 15 (4-Isopropyl-piperazin-1-yl)-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
- (4-Isopropyl-piperazin-1-yl)-{4-(4-isopropyl-piperazin-1-ylmethyl)-phenyl}-methanone;
- 20 (4-Isopropyl-piperazin-1-yl)-{4-[(2-methoxy-ethylamino)-methyl]-phenyl}-methanone;
- (4-Isopropyl-piperazin-1-yl)-[4-(pyridin-2-ylaminomethyl)-phenyl]-methanone;
- (4-Isopropyl-piperazin-1-yl)-{4-[(2-methoxy-1-methyl-ethylamino)-methyl]-phenyl}-methanone;
- 25 (4-Isopropyl-piperazin-1-yl)-{4-[(5-trifluoromethyl-pyridin-2-ylamino)-methyl]-phenyl}-methanone dihydrochloride;
- (4-Isopropyl-piperazin-1-yl)-{4-[(6-trifluoromethyl-pyridin-3-ylamino)-methyl]-phenyl}-methanone dihydrochloride;
- 30 (4-Methyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- (4-Methyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone dihydrochloride;

- (4-sec-Butyl-piperazin-1-yl)-(4-dimethylaminomethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- 5 (4-sec-Butyl-piperazin-1-yl)-(4-phenylaminomethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
- 10 {4-(1-Ethyl-propyl)-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- {4-(1-Ethyl-propyl)-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- {4-(1-Ethyl-propyl)-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;
- 15 {4-(1-Ethyl-propyl)-piperazin-1-yl)-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
- {4-(1-Ethyl-propyl)-piperazin-1-yl)-{4-(decahydro-isoquinolin-2-ylmethyl)-phenyl}-methanone;
- 20 {4-(Benzylamino-methyl)-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
- {4-(Benzylamino-methyl)-phenyl)-{4-(1-ethyl-propyl)-piperazin-1-yl)-methanone; and
- {4-((5-Chloro-pyridin-2-ylamino)-methyl)-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride.
- 25
39. A compound of claim 1 selected from the group consisting of:
- (4-[[Ethyl-(2-methoxy-ethyl)-amino]-methyl]-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone;
- 30 (4-Azepan-1-ylmethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
- (4-Azepan-1-ylmethyl-phenyl)-(4-sec-butyl-piperazin-1-yl)-methanone;

- (4-Azepan-1-ylmethyl-phenyl)-{4-(1-ethyl-propyl)-piperazin-1-yl}-methanone;
- (4-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
- (4-Cyclohexyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- 5 (4-Diethylaminomethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
- (4-Dimethylaminomethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
- 10 (4-Dimethylaminomethyl-phenyl)-{4-(1-ethyl-propyl)-piperazin-1-yl}-methanone dihydrochloride;
- (4-Isopropyl-piperazin-1-yl)-(4-[(2-methoxy-ethyl)-propyl-amino]-methyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- 15 (4-Isopropyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone dihydrochloride;
- (4-Isopropyl-piperazin-1-yl)-(4-thiomorpholin-4-ylmethyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
- 20 (4-Isopropyl-piperazin-1-yl)-{4-[(2-methoxy-ethylamino)-methyl]-phenyl}-methanone;
- (4-Isopropyl-piperazin-1-yl)-[4-(pyridin-2-ylaminomethyl)-phenyl]-methanone;
- 25 (4-Isopropyl-piperazin-1-yl)-{4-[(2-methoxy-1-methyl-ethylamino)-methyl]-phenyl}-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-dimethylaminomethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- 30 (4-sec-Butyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;

- {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- 5 {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;
- {4-(1-Ethyl-propyl)-piperazin-1-yl}-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
- {4-(1-Ethyl-propyl)-piperazin-1-yl}-{4-(decahydro-isoquinolin-2-ylmethyl)-phenyl}-methanone;
- 10 {4-(Benzylamino-methyl)-phenyl}-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride; and
- {4-(Benzylamino-methyl)-phenyl}-{4-(1-ethyl-propyl)-piperazin-1-yl}-methanone.
- 15
40. A compound of claim 1 selected from the group consisting of:
- (4-Azepan-1-ylmethyl-phenyl)-(4-isopropyl-piperazin-1-yl)-methanone dihydrochloride;
- (4-Azepan-1-ylmethyl-phenyl)-(4-sec-butyl-piperazin-1-yl)-methanone;
- 20 (4-Cyclohexyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-Isopropyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone dihydrochloride;
- (4-Isopropyl-piperazin-1-yl}-{4-(3-trifluoromethyl-piperidin-1-ylmethyl)-phenyl}-methanone dihydrochloride;
- 25 (4-sec-Butyl-piperazin-1-yl)-(4-dimethylaminomethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- (4-sec-Butyl-piperazin-1-yl)-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;
- 30 {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride;
- {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-piperidin-1-ylmethyl-phenyl)-methanone; and

{4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone.

41. A compound of claim 1 selected from the group consisting of:
- 5 (4-Azepan-1-ylmethyl-phenyl)-(4-sec-butyl-piperazin-1-yl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
(4-sec-Butyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
{4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-piperidin-1-ylmethyl-phenyl)-methanone;
- 10 {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
(4-sec-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride; and
- 15 {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride.
42. A pharmaceutical composition, comprising a compound of claim 1 and a pharmaceutically-acceptable excipient.
- 20 43. A compound of claim 1 isotopically-labelled to be detectable by PET or SPECT.
44. A method of inhibiting histamine H₃ receptor activity in a subject, comprising administering an effective amount of a compound of claim 1 to a subject in need of such inhibition of histamine H₃ receptor activity.
- 25 45. A method of treating a subject having a disease or condition modulated by histamine H₃ receptor activity, comprising administering to the subject a therapeutically effective amount of a compound of claim 1.
- 30 46. A method of claim 45, wherein said disease or condition is selected from the group consisting of sleep/wake disorders, arousal/vigilance

- disorders, migraine, asthma, dementia, cognitive dysfunction, neurogenic inflammation, mild cognitive impairment (pre-dementia), Alzheimer's disease, epilepsy, narcolepsy, eating disorders, obesity, motion sickness, vertigo, attention deficit hyperactivity disorders, learning disorders, memory retention disorders, schizophrenia, substance abuse, bipolar disorders, manic disorders and depression, nasal congestion, itch, allergic rhinitis, and upper airway allergic response.
- 5
- 10 47. A method for treating a disease or condition modulated by at least one receptor selected from the histamine H₁ receptor and the histamine H₃ receptor, said method comprising (a) administering to a subject a jointly effective amount of a histamine H₁ receptor antagonist compound, and (b) administering to the subject a jointly effective amount of a compound of claim 1, said method providing a jointly therapeutically effective amount of said compounds.
- 15
48. The method of claim 47 wherein the histamine H₁ receptor antagonist and the compound of claim 1 are present in the same dosage form.
- 20
49. A method for treating diseases or conditions modulated by at least one receptor selected from the histamine H₂ receptor and the histamine H₃ receptor in a subject, comprising (a) administering to the subject a jointly effective amount of a histamine H₂ receptor antagonist compound, and (b) administering to the subject a jointly effective amount of a compound of claim 1, said method providing a jointly therapeutically effective amount of said compounds.
- 25
50. The method of claim 39 wherein the histamine H₂ receptor antagonist and the compound of claim 1 are present in the same dosage form.
- 30
51. A method for treating one or more disorders or conditions selected from the group consisting of sleep/wake disorders, narcolepsy, and

arousal/vigilance disorders, comprising administering to a subject a therapeutically effective amount of a compound of claim 1.

52. A method for treating attention deficit hyperactivity disorders (ADHD),
5 comprising administering to a subject a therapeutically effective amount of a compound of claim 1.
53. A method for treating one or more disorders or conditions selected from
10 the group consisting of dementia, mild cognitive impairment (pre-dementia), cognitive dysfunction, schizophrenia, depression, manic disorders, bipolar disorders, and learning and memory disorders, comprising administering to a subject a therapeutically effective amount of a compound of claim 1.
- 15 54. A method for treating or preventing upper airway allergic response, itch, nasal congestion, or allergic rhinitis, comprising administering to a subject a therapeutically effective amount of a compound of claim 1.
- 20 55. A method for studying disorders mediated by the histamine H₃ receptor, comprising using an ¹⁸F-labeled or ¹¹C-labelled compound of claim 1 as a positron emission tomography (PET) molecular probe.